

CONCEPT

DETAILED PARAMETERS

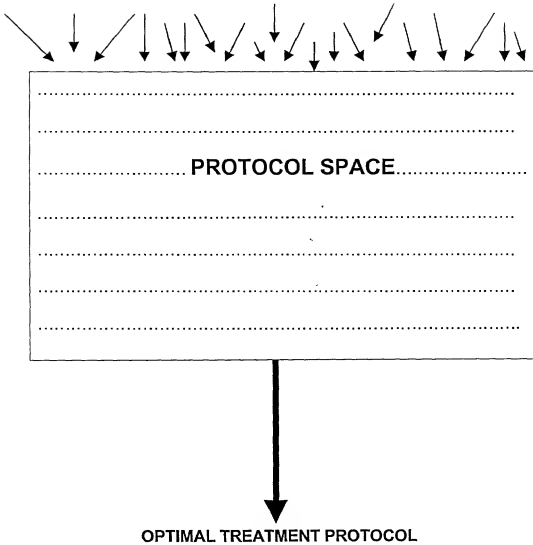


Fig. 1

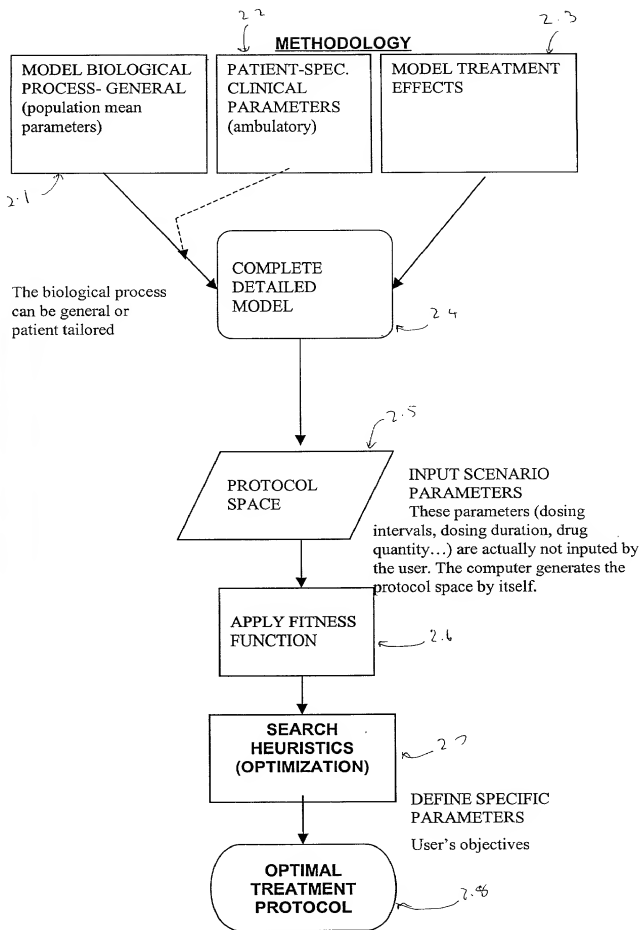


Fig. 2

METHODOLOGY (2)

Attempting to optimize some instance of
a chemotherapy problem with a given
set of solutions...

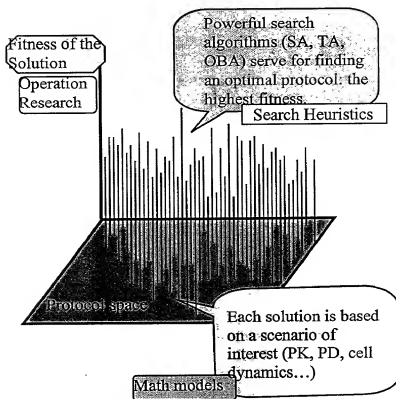


Fig. 2a

09827229.040601

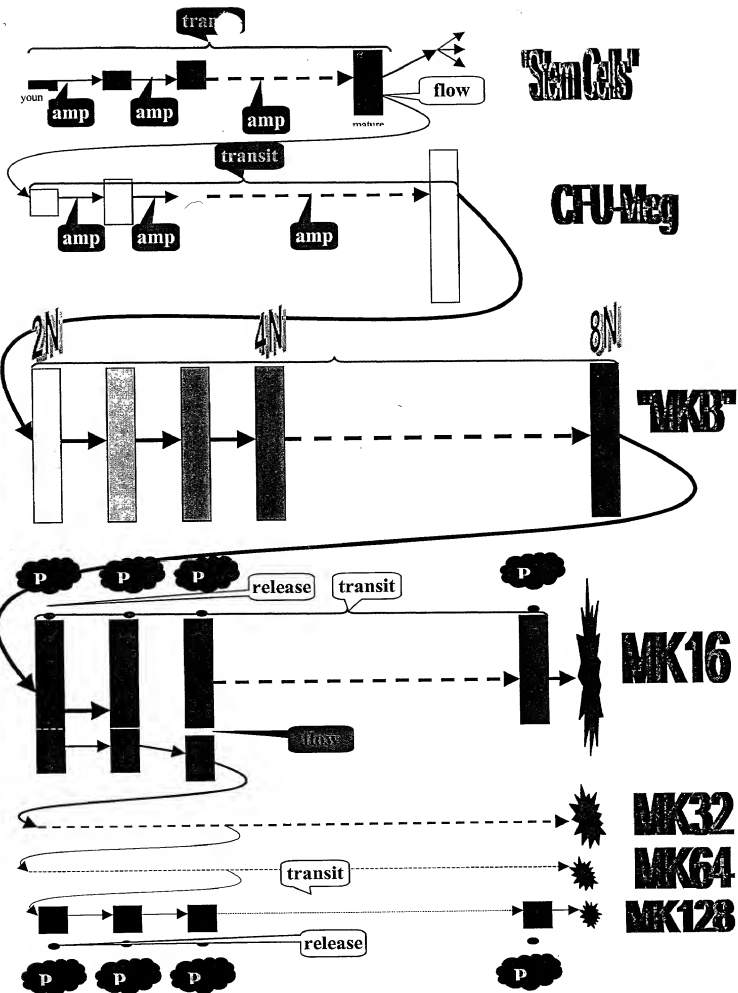


Fig. 3

09527220 040501

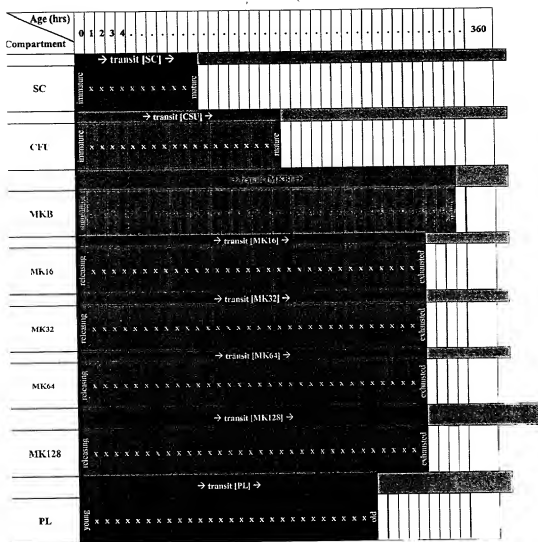


Fig 4

00527220 0416001
100910 62242860

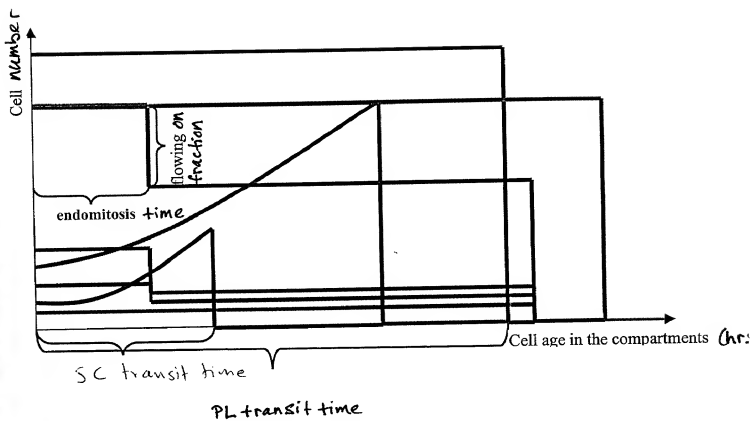


Fig. 5

Fig. 6

Fig. 6

The graph displays the average number of nodes in the network over time for various configurations. The Y-axis is labeled from 0.00 to 7000.00 in increments of 1000.00. The X-axis is labeled from 0.00 to 0.50 in increments of 0.10. There are approximately 15 data series represented by different markers and line styles. Key observations include:

- A series with open circles starts at ~5000, peaks at ~6300 around x=0.05, and then drops to ~3800 by x=0.15, remaining relatively stable thereafter.
- A series with open squares starts at ~4000, drops sharply to ~2900 at x=0.05, and then fluctuates between 2000 and 3500.
- A series with open triangles starts at ~4000 and decreases steadily to ~1500 by x=0.15, then continues to decrease more slowly.
- A series with open diamonds starts at ~4000 and increases steadily to ~7000 by x=0.50.
- Several series remain relatively flat, clustered between 1000 and 2000 nodes.
- One series with solid circles starts at ~4000, drops to ~1000 at x=0.15, and then rises to ~2000 by x=0.50.

Fig. 7

Simulations showing that if the protocol is pre-calculated then a similar or a higher efficacy can be obtained using 4-fold reduced total dose of TPO.

TPO use in healthy donors:

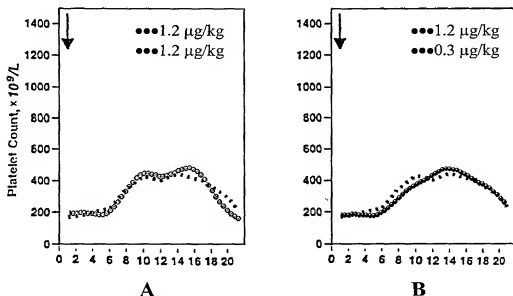


Fig. 8: TPO given to healthy donors- Results of TPO clinical trials from recent research on healthy platelet donors, as compared to our computer simulation results. Arrows indicate the start of TPO treatment. (A) Comparison of experimental data from published articles¹ (black) and our model simulation (green), in both TPO was given as a single IV dose of 1.2 µg/kg on day 0. (B) Comparison of the same experimental data (black) and our proposed TPO administration protocol; the total dose in the simulated protocol was 0.3 µg/kg (blue).

TPO use in patients receiving chemotherapy:

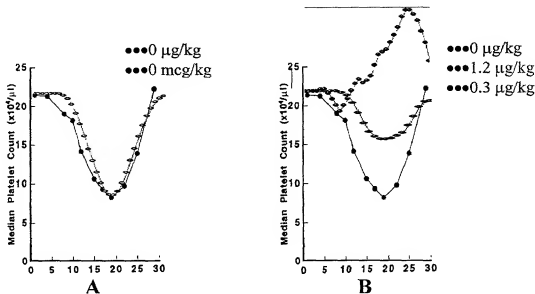


Fig. 9: TPO with chemotherapy- (A) Results of clinical trials from recent research on thrombocytopenia induced in patients receiving single carboplatin chemotherapy⁷ on day 0 (black), as compared to our model simulation of these results (green). (B) The same experimental data (black); simulations of the same experiment, with addition of "conventional" TPO protocol of a single IV dose of 1.2 µg/kg on day 0 (olive); simulations of the same experiment under our proposed protocol that totals 0.3 µg/kg (blue).

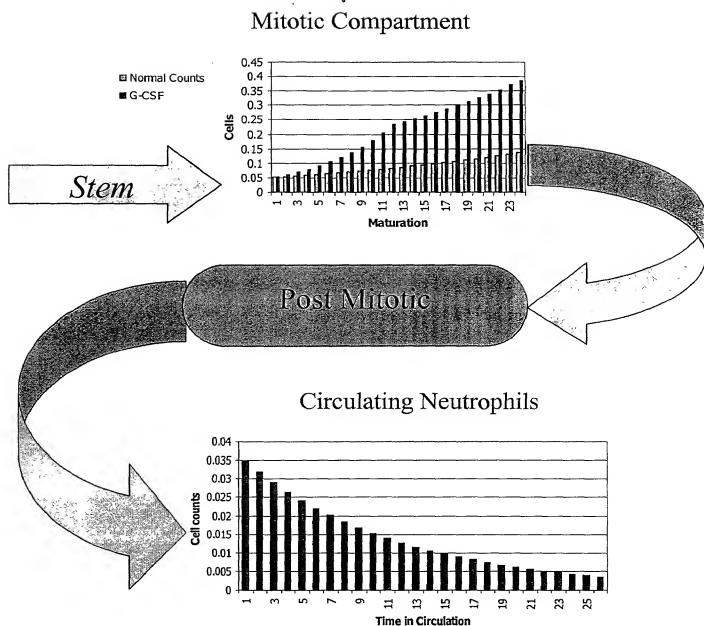


Fig. 10

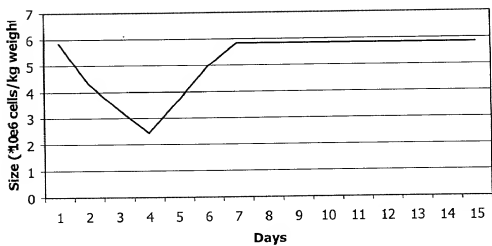


Fig. 11

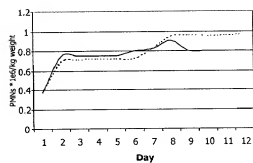


Fig. 12a

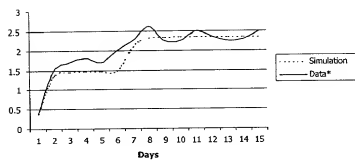
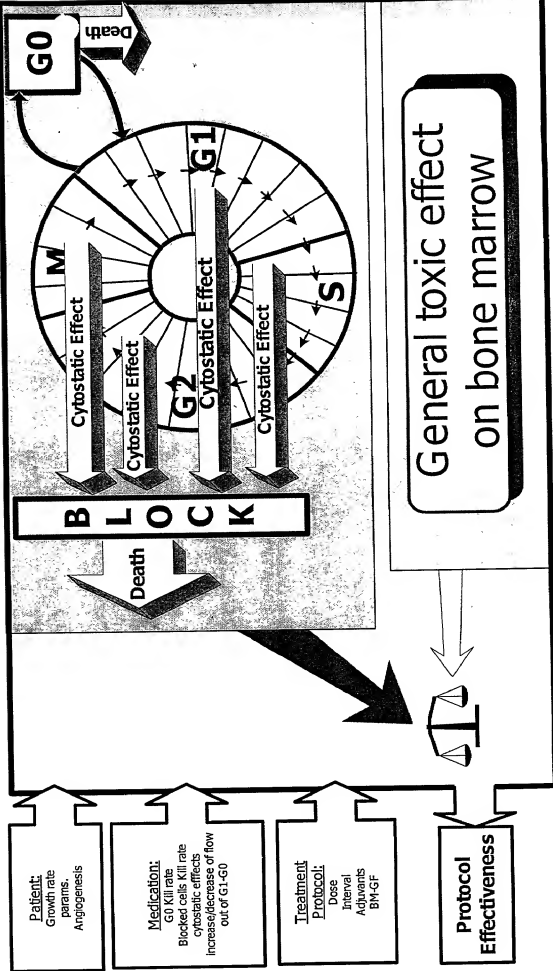


Fig. 12b



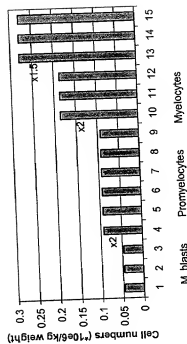


Fig 14. Simulated mitotic compartment age distribution and differentiation values in untreated humans. Each bar represents a grouping of 8 cohorts of one hour. Amplification is noted at the place of occurrence.

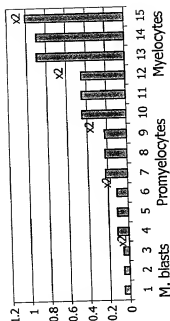


Fig. 15. Simulated mitotic compartment age distribution and amplification values in humans treated with 300 µg of G-CSF after 15 days. Each bar represents a grouping of 8 cohorts of one hour. Amplification is noted at the place of occurrence. Note, that the last hourly cohort of the Myelocytes undergoes mitosis, but its effects are dampened in this graph due to the 8h grouping.